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MODERN CONCEPTS OF CARDIOVASCULAR DISEASE

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Clinical Features and Diagnosis of Primary Myocardial Disease (II)*†

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HEMODYNAMIC FINDINGS

A considerable number of patients with various forms of primary myocardial disease (PMD) have had right heart catheterization, left heart catheterization, or both.[2, 4-7, 10, 24-27] The findings depend upon the type of the disease and its status at the time studied. Other than giving a better understanding of the pathophysiology of the disease, these procedures provide diagnostic information in excluding conditions in the differential diagnosis which, if present, might be helped by surgery or other specific therapy. The value and limitations will be discussed under the section, "Differential Diagnosis."

In the patients with subacute and chronic myocarditis (including those with fibroelastosis and so-called idiopathic hypertrophy and failure) in which the disease is advanced and complicated by failure, the findings have been rather uniform.[2] The important findings in these cases are: (1) a low and relatively fixed cardiac output; (2) increased arteriovenous oxygen difference but absence of intra- or extracardiac shunt; (3) elevated systolic, mean, and usually end-diastolic pressures in the right ventricle without a systolic gradient across the pulmonary valve, elevated mean pulmonary artery, and pulmonary capillary pressures; (4) elevated end-diastolic pressure in the left ventricle and, when the mitral valve is incompetent, elevation of the systolic and end-diastolic pressures in the left atrium but without a diastolic gradient across the mitral valve indicative of mitral stenosis; (5) elevation of the systolic and end-diastolic pressures in the right atrium when tricuspid incompetency is present; (6) abnormal contours of the ventricular and atrial pressure curves, characterized by a loss of the prompt systolic ejection curves, as produced by the normal functioning ventricle.

Catheterization findings in PMD, which terminate in diffuse myocardial fibrosis and myocardial restriction, have been studied; present findings, in most instances, closely simulate those of the constrictive pericardium. The author agrees with others[24, 28] that usually the two conditions cannot be adequately differentiated by the results of hemodynamic studies.

The hemodynamic findings in asymmetrical hypertrophy of the myocardium have been reported under the titles of "subaortic stenosis,"[29] "functional aortic stenosis,"[30] "familial muscular subaortic stenosis,"[31] and "obstructive cardiomyopathy simulating aortic stenosis."[32] When severe failure develops in this group, the catheterization findings may be similar to those with diffuse muscle disease, but earlier the im-

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portant findings are the pressure gradients in the outflow tracts of the left and right ventricles simulating organic valve lesions.

SPECIAL DIAGNOSTIC STUDIES

Today, there exists a wide spectrum of diagnostic laboratory studies which may be employed to assist in the differential diagnosis of PMD from other forms of circulatory diseases and to identify the specific etiological factor involved. Myocardial biopsy, obtained by a transthoracic needle,[33] or by myocardial tissue obtained by surgical exploration, has been performed without difficulty and in some instances has provided an etiological diagnosis, as well as confirmation of the presence of a lesion in the myocardium. Further experience is necessary to establish the value of this procedure. The diagnosis of myocardial sarcoidosis has been made from myocardial biopsy. PMD of this etiology is being suspected and recognized more frequently,[34] and a positive diagnosis by biopsy would permit a basis for beneficial treatment with steroids. Additional biochemical and enzyme studies of biopsy material might give additional diagnostic information. Use of selected enzyme studies in suspected acute and subacute cases are helpful at times, but the findings are not specific. The absence of characteristic enzyme findings, as seen in an acute myocardial infarction, may be helpful in differential diagnosis. The laboratory studies, which might be employed in the determination of etiology of acute myocarditis, are many and should be determined by the clinical and epidemological features. For example: a case of acute myocarditis in Brazil might logically have a blood smear in search of the trypanosomes of T. cruzi; a subacute or chronic case of myocarditis in the same locality might have a complement-fixation test (Machado-Guerreiro reaction) for aid in the diagnosis of chronic Chagas' disease. In many instances of acute myocarditis, the opportunity to obtain diagnostic etiological studies has passed by the time the clinical features of the myocarditis are recognized. Even the use of serological tests are rendered useless by the absence of earlier specimens for comparison of titers.

DIFFERENTIAL DIAGNOSIS

The wide spectrum of etiological factors, clinical and pathological features, variations in clinical course, and associations with other systemic and generalized diseases, produce multiple problems in the differential diagnosis of PMD. Some of the common problems are reviewed briefly.

CONFUSION WITH ORGANIC VALVULAR HEART DISEASE

The large group with subacute or chronic myocarditis, including the so-called idiopathic cardiomegalies, etc, in which cardiomegaly, failure, and cardiac murmurs from dilatation and incompetency of the atrioventricular valves occur, are often confused with organic valvular heart disease, especially mitral and aortic valve lesions and occasionally with tricuspid lesions and congenital defects. The characteristics of the murmurs of PMD with improvement from failure and decrease in cardiac dilatation, as described under auscultatory findings, is most helpful. Isolated chamber enlargement is more common in organic valve disease, whereas generalized cardiomegaly is the rule in PMD. Calcification of the diseased valves is frequent in organic valve disease, and absent in valvular incompetency associated with PMD or in those with obstructive asymmetrical hypertrophy. Hemodynamic findings from right and left heart catheterization are helpful in identifying gradients across stenotic valves, but do not always differentiate organic and functional valvular insufficiencies. Chronic valvular heart disease, complicated by bacterial endocarditis and extensive embolic myocarditis and myocardial failure, may present very difficult problems in differential diagnosis. The same is true of rheumatic valvular heart disease complicated by severe active rheumatic myocarditis, or lupus, with both endocardial valvular lesions and myocardial lesions. Specific findings of a positive blood culture in subacute bacterial endocarditis (SBE), a rising titer in the antistreptolysin titer in rheumatic carditis or specific hematological features of lupus are valuable in the differential diagnosis which may not be made from other clinical features. Occasionally, in children, PMD has been confused with congenital defects of the tricuspid valve and mitral valves (Ebstein type of abnormality).

The next types of PMD which are difficult to differentiate from organic valvular heart diseases are those with idiopathic hypertrophy, with or without endomyofibrosis, in which the changes are limited primarily to the left ventricle, and those with obstructive hypertrophy involving the outflow tracts, chiefly that of the left ventricle. The differential diagnosis of these types is quite difficult, especially in the early stage before congestive failure develops.

Cardiac murmurs, size and shape of chamber, enlargement on clinical and radiological examination, and the electrocardiographic findings, may simulate in every respect those of organic valvular disease, especially that of the aortic valve. Hence, they have been called functional or pseudoaortic stenosis. Left heart catheterization findings are helpful in differentiating those with generalized ventricular hypertrophy and dilatation from organic valve disease with secondary muscle hypertrophy, but may not be of much help in differentiating the obstructive outflow tract hypertrophies from organic valvular disease. Braunwald[35] has recently pointed out clinical and hemodynamic features which might prove helpful in differentiation. A history of other members in the family with a similar type of heart lesion would favor the diagnosis of idiopathic obstructive hypertrophy; multiple instances have been observed in families.[31, 35, 36]

CONFUSION WITH PERICARDIAL DISEASE

There are two forms of PMD which at times are confused with pericardial disease: (1) Acute and subacute myocarditis with a greatly enlarged globular cardiac silhouette from failure and dilatation, poor myocardial contractions on fluoroscopy, and low voltage in the electrocardiogram, are at times extremely difficult to differentiate from a pericarditis with effusion. (2) Chronic myocarditis, with diffuse fibrosis, and endomyofibrosis or amyloidosis of the myocardium and a normal-sized heart or only moderate cardiomegaly, poor myocardial contractility on fluoroscopy, and hemodynamic findings indicative of restrictive diastolic filling on cardiac catheterization, presents a most difficult problem of differential diagnosis from constrictive pericardial disease with secondary impairment of myocardial function and restriction of cardiac action. There are many minor points in the clinical features of each of these myocardial and pericardial diseases which give a basis for definite differentiation; at times special studies are valuable. However, pericardial paracentesis or surgical exploration is often necessary to exclude pericardial effusion, or surgical exploration is necessary to exclude a constrictive pericardium.

CONFUSION WITH CORONARY DISEASE

Differential diagnosis of PMD and myocardial fibrosis and insufficiency secondary to coronary disease results from the presence of many clinical features which are common to both. Myocardial ischemia, necrosis, fibrosis, cardiac enlargement, and failure due to coronary atherosclerosis, develop at times in a rather silent manner without either angina, episodes of myocardial infarction, or localized ECG abnormalities. When such patients are seen late in their clinical course, with biventricular failure, mitral valve incompetency from either a dilated left ventricle or damage to the papillary muscles, the clinical picture may closely simulate PMD with cardiomegaly, biventricular failure, and atrioventricular valve incompetencies. Arrhythmias, conduction disorders, and gallop rhythm are common to both. As a rule, only careful evaluation of the history and clinical course provides diagnostic help. Both coronary and noncoronary myocardial lesions can result in diffuse myocardial fibrosis with a small heart, but with failure by restriction of diastolic filling.[28]

Again, the patient who develops conduction disorders, such as high-grade or complete A-V block, bundle-branch block, or ventricular arrhythmias, either acutely or asymptomatically as found on routine examination, may have either PMD or coronary disease as the underlying cause. The patient with PMD is more likely to have associated cardiomegaly. Localized areas of ischemia and myocardial damage resulting from coronary disease sufficient to produce these conduction disorders and arrhythmias need not be large and the underlying coronary disease can be limited to small areas of the coronary bed rather than be diffuse in nature. Coronary disease may occur at an early age, especially in males, and myocarditis, amyloidosis, etc., occur in the aged; hence age is not always reliable in differential diagnosis. The anomalous coronary artery, with origin of the left coronary artery from the pulmonary artery, usually seen in infants, frequently appears with cardiomegaly and failure and simulates acute and subacute myocarditis.

Finally, acute myocarditis, either of specific etiology or of an idiopathic type, occurring in the age group where coronary disease is frequent may, in its symptoms and clinical course, present many similar features to that of an acute infarction, including confusing electrocardiographic and enzyme abnormalities. Careful attention must be given to the details of clinical history and development to make a correct differential diagnosis.

CONFUSION WITH PULMONARY HYPERTENSIVE CARDIOVASCULAR DISEASE WITH FAILURE

Pulmonary hypertension, especially of the primary or idiopathic type, may develop in-

sidiously and appear eventually with severe failure, low cardiac output, dilated heart, relative tricuspid incompetency, and arrhythmias. Cardiac catheterization is not always a desirable and safe procedure where there are features suggesting severe pulmonary hypertension, and when performed the results may not provide a basis for differential diagnosis. The severity of pulmonary hypertension, as found in PMD, may equal that found in primary pulmonary hypertension. The roentgenological and electrocardiographic features found late in the course may be similar. Early in the course, helpful features in identifying pulmonary hypertension as the basic cardiovascular problem are isolated right ventricular hypertrophy, enlargement of the pulmonary artery and its main branches, with decreased vascularity of the peripheral lung fields.

To sum up, prompt recognition of the clinical features of PMD in patients with heart disease may lead to an early diagnosis, indicate specific etiology, and permit better management with reduction of morbidity and mortality of the disease. Furthermore, early recognition will provide an opportunity for more effective clinical investigation and research, not only in the fields of etiology and prevention, but also in relatively unexplored fields, such as the nature and relationship of the underlying histochemical, enzymal, nutritional, and physical derangements of the myocardium to myocardial insufficiency.

Burch[37] has pointed out the nature of the mechanical disadvantages provided by cardiac dilatation, which is a clinical feature common to most forms of PMD. Recently, Grant[38] called our attention to the investigators in Western Germany who have used mathematical methods in the study of cardiac morphology and the effects of cardiac dilatation and hypertrophy on the heart. It is refreshing to see something new added to our understanding of the diseases of the myocardium besides the histological changes already noted by Virchow a century ago. The prompt clinical recognition of cardiac dilatation and the clinical symptoms of myocardial insufficiency, as defined by Christian, followed by the institution of appropriate measures to overcome dilatation before it becomes irreversible and complicated by hypertrophy and intractable failure, would go a long way in preventing disability and early death from PMD, regardless of its specific etiology.

REFERENCES

1. **Christian, H. A.:** Clinically the myocardium. Arch. Int. Med. 86:491, 1950.
2. **Mattingly, T. W.:** Clinical and hemodynamic features of primary myocardial disease. Tr. Am. Clin. & Climatol. A. 70:132, 1958.
3. **Harvey, W. P., and Perloff, J. K.:** Auscultatory findings in primary myocardial disease. Am. Heart J. 61:199, 1961.
4. **Fowler, N. O., Gueron, M., and Rowlands, D. T., Jr.:** Primary myocardial disease. Circulation 23:498, 1961.
5. **Brigden, W.:** Uncommon myocardial diseases: Non-coronary cardiomyopathies. Lancet 273 (7007 & 8):1179 and 1243, 1957.
6. **Hickie, J. B., and Hall, G. V.:** Cardiomyopathies: Report of fifty cases. Australasian Ann. Med. 9:258, 1960.
7. **Goodwin, J. F., Gordon, H., Hollman, A., and Bishop, M. B.:** Clinical aspects of cardiomyopathy. Brit. Med. J. 1:69, 1961.
8. **Blankenhorn, M. A., and Gall, E. A.:** Myocarditis and myocardosis. Circulation 13:217, 1956.
9. **Evans, W.:** Familial cardiomegaly. Brit. Heart J. 11:68, 1949.
10. **Spodick, D. H., and Littmann, D.:** Idiopathic myocardial hypertrophy. Am. J. Cardiol. 1:610, 1958.
11. **Teare, D.:** Asymmetrical hypertrophy of the heart in young adults. Brit. Heart J. 20:1, 1958.
12. **Thomas, W. A., Randall, R. V., Bland, E. F., and Castleman, B.:** Endocardial fibroelastosis: Factor in heart disease of obscure etiology: Study of 20 autopsied cases in children and adults. New England J. Med. 251:327, 1954.
13. **Fisher, E. R., and Davis, E. R.:** Myocarditis with endocardial elastomyofibrosis (EEMF). Am. Heart J. 56:537, 1958.
14. **Menion, W. C.:** Scientific exhibits: Myocarditis, a frequent complication of systemic diseases. A.M.A. Arch. Path. 61:329, 1956.
15. **Saphir, O.:** Myocarditis. Am. Heart J. 57:639, 1959.
16. **de la Chapelle, C. E., and Kossmann, C. E.:** Myocarditis. Circulation 10:747, 1954.
17. **Kline, I. K., and Saphir, O.:** Chronic pernicious myocarditis. Am. Heart J. 59:681, 1960.
18. **Fisher, E. R., and Davis, E. R.:** Observations concerning the pathogenesis of endocardial thickening in the adult heart. Am. Heart J. 56:553, 1958.
19. **Still, W. J. S.:** Endocardial fibroelastosis. Am. Heart J. 61:579, 1961.
20. **Wagner, H. N., Jr., McAfee, J. G., and Mozley, J. M.:** Diagnosis of pericardial effusion by radioisotope scanning. Circulation 22:828, 1960.
21. **Schiebler, G. L., Adams, P., Jr., and Anderson, R. C.:** Familial cardiomegaly in association with the Wolff-Parkinson-White syndrome. Am. Heart J. 58:113, 1959.
22. **Levine, S. A., and Harvey, W. P.:** Clinical Auscultation of the Heart, ed. 2. Philadelphia, W. B. Saunders Co., 1959.
23. **Burchell, H. B.:** Unusual causes of heart failure. Circulation 21:436, 1960.
24. **Balchum, O. J., McCord, M. C., and Blount, S. G., Jr.:** Clinical and hemodynamic pattern in nonspecific myocarditis: Comparison with other entities also impairing myocardial efficiency. Am. Heart J. 52:430, 1956.
25. **Lynfield, J., Gasul, B. M., Luan, L. L., and Dillon, R. F.:** Right and left heart catheterization and angiocardiographic findings in idiopathic cardiac hypertrophy with endocardial fibroelastosis. Circulation 21:386, 1960.
26. **Nye, R. E., Lovejoy, F. W., Jr., and Yu, P. N.:** Clinical and hemodynamic studies of myocardial fibrosis. Circulation 16:332, 1957.
27. **Robin, E. D., and C. S. Burwell:** Hemodynamic aspects of diffuse myocardial fibrosis. Circulation 16:730, 1957.
28. **Burwell, C. S., and Robin, E. D.:** Diagnosis of diffuse myocardial fibrosis. Circulation 20:606, 1959.
29. **Brachfeld, N., and Gorlin, R.:** Subaortic stenosis: A revised concept of the disease. Medicine 38:415, 1959.
30. **Morrow, A. G., and Braunwald, E.:** Functional aortic stenosis: Malformation characterized by resistance to left ventricular outflow without anatomic obstruction. Circulation 20:181, 1959.
31. **Brent, L. B., Aburano, A., Fisher, D. L., Moran, T. J., Myers, J. D., and Taylor, W. J.:** Familial muscular subaortic stenosis: Unrecognized form of "idiopathic heart disease" with clinical and autopsy observations. Circulation 21:167, 1960.
32. **Goodwin, J. F., Hollman, A., Cleland, W. P., and Teare, D.:** Obstructive cardiomyopathy simulating aortic stenosis. Brit. Heart J. 22:403, 1960.
33. **Sutton, D. C., and Sutton, G. C.:** Needle biopsy of the human ventricular myocardium: Review of 54 consecutive cases. Am. Heart J. 60:364, 1960.
34. **Porter, G. H.:** Sarcoid heart disease. New England J. Med. 263:1350, 1960.
35. **Braunwald, E., Morrow, A. G., Cornell, W. P., Ayers, M. M., and Hilbish, T. F.:** Idiopathic hypertrophic subaortic stenosis: Clinical, hemodynamic and angiographic manifestations. Am. J. Med. 29:924, 1960.
36. **Hollman, A., Goodwin, J. F., Teare, D., and Renwick, J. W.:** A family with obstructive cardiomyopathy (asymmetrical hypertrophy). Brit. Heart J. 22:449, 1960.
37. **Burch, G. E., and Walsh, J. J.:** Cardiac enlargement due to myocardial degeneration of unknown cause: Preliminary report on effect of prolonged bed rest. J.A.M.A. 172:207, 1960.
38. **Grant, R. P.:** Quantitative morphology: New approach to cardiac pathology. Circulation 23:645, 1961.